

Module 6 – Green Chemistry in the Real World II



Global Greenchem
Innovation & Network Program

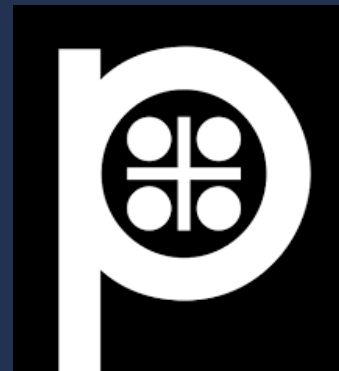


Green Chemistry Toolkit



Center for Green Chemistry &
Green Engineering at Yale

Companies that do Green Chemistry!





Provivi



Why do we need pesticides?



- Pesticides of many different kinds are important for global food security.
- Pests of different kinds affect almost all staple foods around the world.



What kind of pesticides are there?

TYPES OF PESTICIDES



FUNGICIDES



HERBICIDES



BACTERICIDES



NEMATICIDES



AVICIDES



RODENTICIDES



INSECTICIDES



ALGICIDES



MOLLUSCICIDES



OVICIDES



Insecticides

- Insecticides are the kind of pesticides specialized to control the effects of insects.

INSECTICIDES AND HOW THEY WORK

Farmers have used synthetic insecticides for decades to protect crops from pests. People also use some in their gardens and on pets. Here we look at some families of insecticides and how they work.

INSECTICIDE EXPOSURE ROUTES



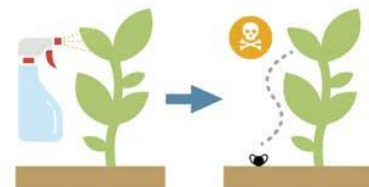
Systemic Insecticides

Systemic insecticides are usually applied to the soil and spread through the entire plant. Insects ingest the insecticide when they eat the plant. These compounds can also work upon contact.



Contact Insecticides

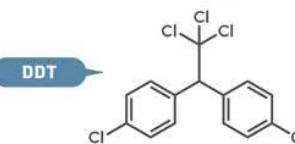
Contact insecticides kill insects when they come in direct contact with the molecules.



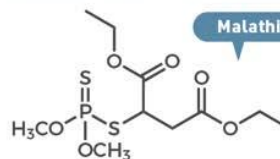
SELECTED SYNTHETIC INSECTICIDE FAMILIES

Organochlorines

These affect either sodium or chloride channels in nerve cells. Many are now restricted or banned globally because they persist in the environment.



Malathion

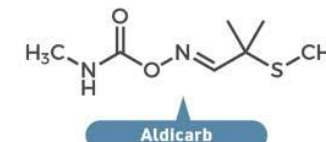


Organophosphates

These insecticides overstimulate the nervous system by irreversibly stopping the breakdown of acetylcholine. The compounds also affect humans and other animals, and their use is restricted.

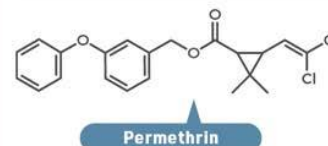
Carbamates

Like organophosphates, these molecules block the breakdown of acetylcholine. Unlike organophosphates, their effects are reversible, so they are less toxic to humans and animals.



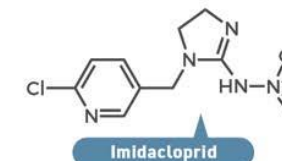
Pyrethroids

This class holds nerve cells' sodium channels open. They mimic pyrethrins, natural compounds in chrysanthemums. Pyrethroids don't harm humans and most mammals but are toxic to cats.



Neonicotinoids

These kill insects by binding to acetylcholine receptors, thereby overstimulating insects' nervous systems. Some research suggests that neonicotinoids may harm honeybees.



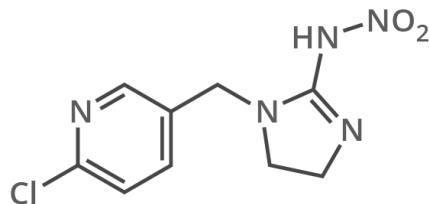
PERIODIC GRAPHICS

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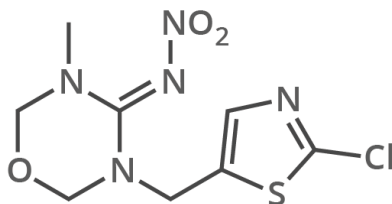


NEONICOTINOID PESTICIDES - THE FACTS

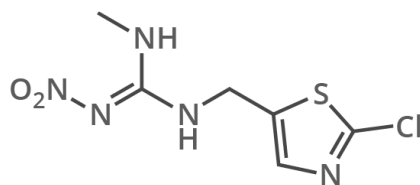
The use of neonicotinoid pesticides has been a contentious issue in recent years. They account for around 25% of the global agrochemical market, but have also been linked with negative environmental effects. This graphic looks at how they work, and the nature of the concerns surrounding them.



IMIDACLOPRID



THIAMETHOXAM



CLOTHIANIDIN



1980s

Decade in which neonicotinoid pesticides first developed

120

Number of countries in which neonicotinoids are registered



Now used more than any other class of insecticide.

HOW DO NEONICOTINOIDS WORK?



Can be added to irrigation water, then taken up & spread through plant tissues. Also used in seed treatments.



ACh

Bind to nicotinic receptors for the neurotransmitter acetylcholine in the insect central nervous system.



This leads to overstimulation and blocking of the receptors, leading to paralysis and eventual death.

Neonicotinoids pesticides are effective against a wide range of crop pests. They are the most widely used insecticides in the world, accounting for roughly 25% of all insecticide use. Median lethal doses vary depending on the size of the insect, ranging from less than 1 nanogram to almost 90 nanograms per insect. Mammals also have the receptors neonicotinoids bind to, but they bind to them less strongly than in insects, so neonicotinoid mammalian toxicity is much lower.

ENVIRONMENTAL CONCERNS



- Can accumulate in soil; low concentrations found in nectar of treated crops.
- Linked as contributors to honey bee colony decline. However, this is still inconclusive, and subject to continued research and conflicting interpretations.
- Increasing evidence of effects on non-target organisms. Negative impacts on monarch butterfly populations in the USA have recently been suggested.
- Use has been partially restricted in the EU since 2013. However, some have suggested this has merely led to increased use of older, harsher pesticides.



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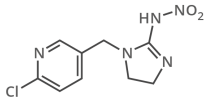


Neonicotinoids are broadband Insecticides

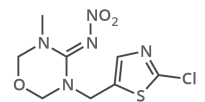


NEONICOTINOID PESTICIDES - THE FACTS

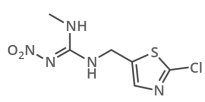
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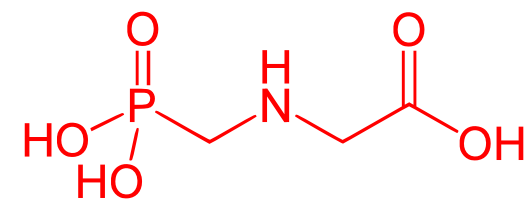
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Now used more than any other class of insecticide.

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- While Neonicotinoids are broadspectrum insecticides, **glyphosate** is a broadspectrum herbicide (Round-Up).



Pesticides and broadband, a big problem

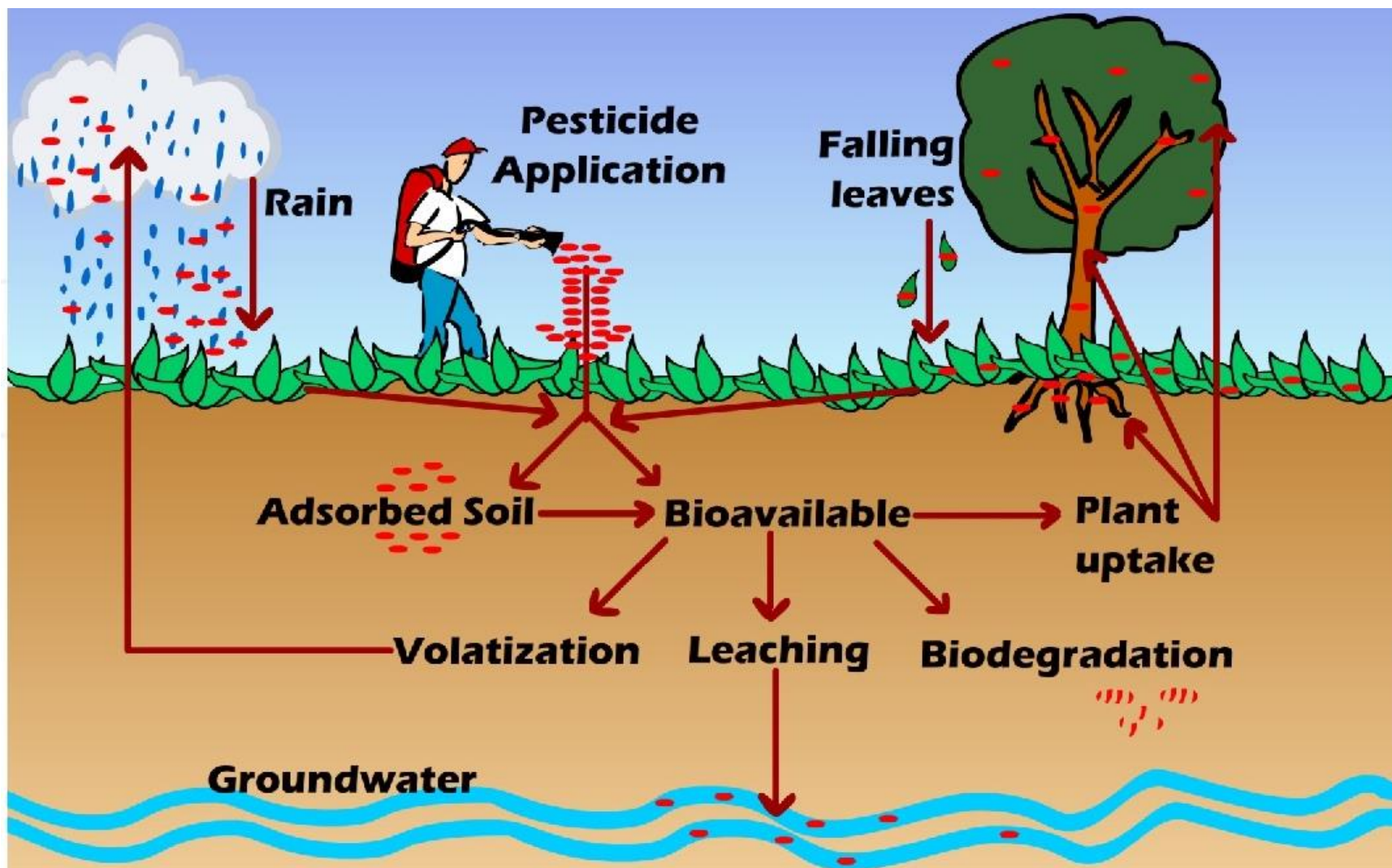


- Pesticides that are broadly acting and are persistent are a special harm for entire ecosystems.
- Bee populations are suffering due to the widespread use of different pesticides (not only insecticides).

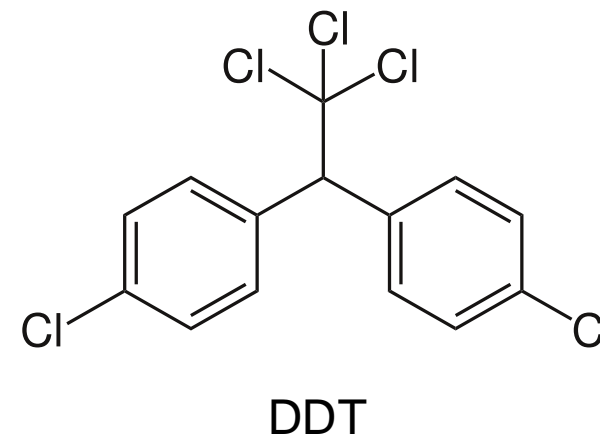
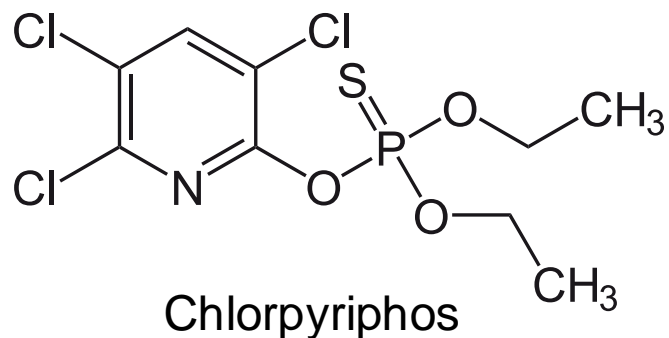
Modern pesticides are developed with a focus on highly **specific activity**, **low toxicities**, and **good degradability**.



Persistent pesticides are a real problem



Persistent pesticides are a real problem



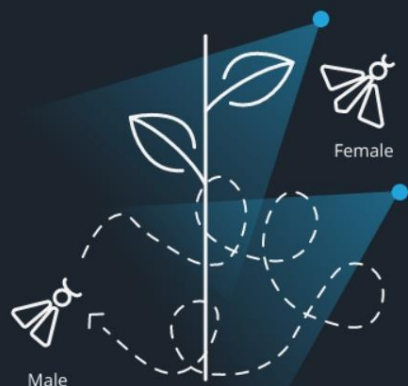
- Since pesticides are usually applied in vast areas, it is especially problematic if they are persistent and do not biodegrade easily.
- DDT and Chlorpyrifos are only two examples of persistent insecticides, so called Persistent Organic Pollutants (POPs).



Provivi's Approach

► Pheromones

Insects produce pheromones to communicate with other insects, helping them mate, find food, and escape predators. Female insects usually release sex pheromones to attract a male for mating.

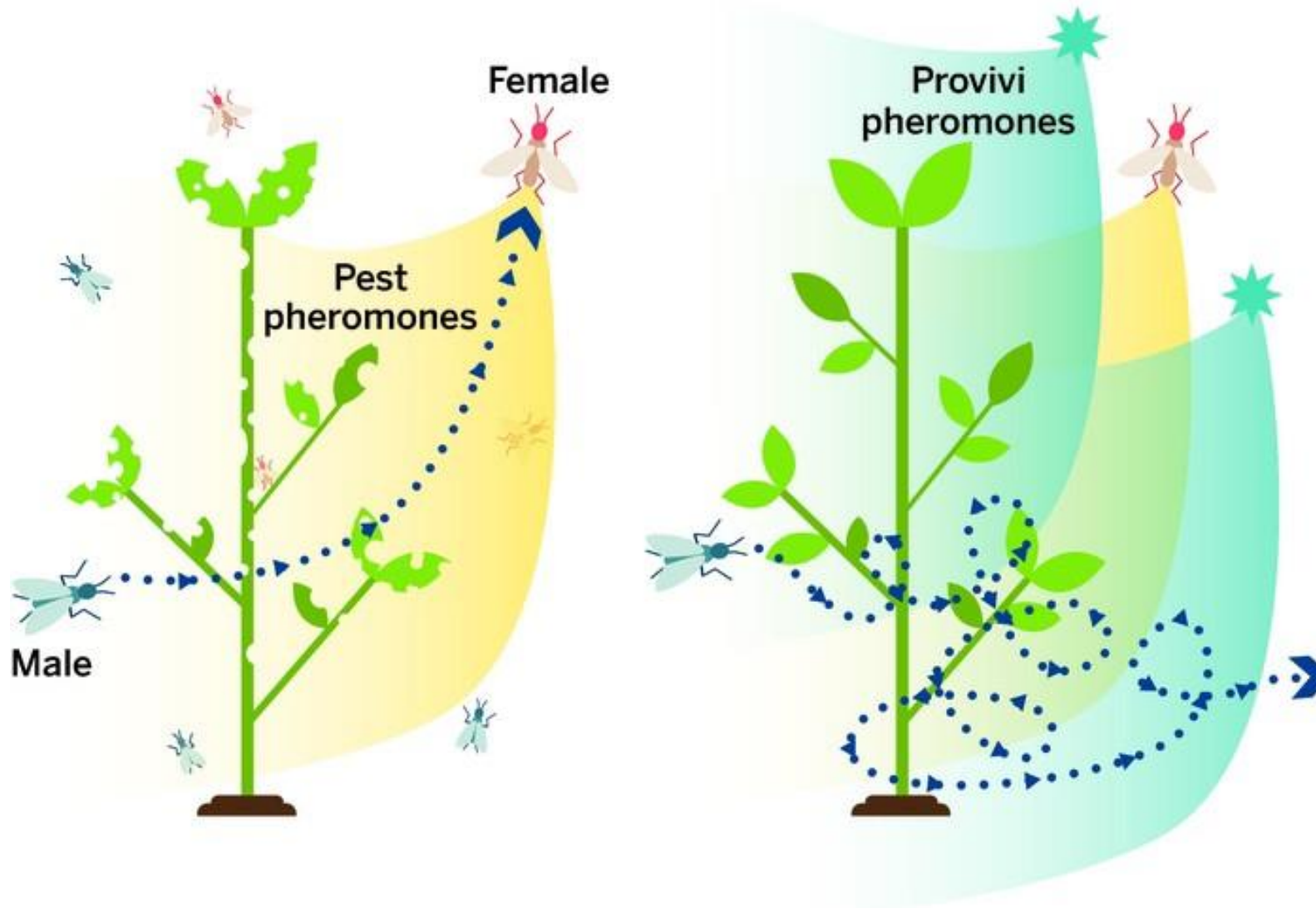


► Synthetic Pheromones

By saturating an environment with artificially synthesized female sex pheromones, male insects are unable to find female insects, thus disrupting the mating process.



Provivi's Approach



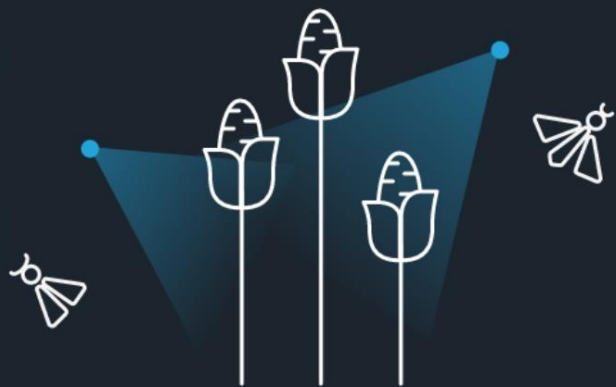
- The synthesis and application of the insect-(pest)-specific pheromone will mislead the male of finding the female insect.



Provivi's Approach

▶ Mating Disruption

Synthesizing pheromones to prevent reproduction is called mating disruption. Unlike traditional insecticides, mating disruption does not kill insects and only results in less offspring in the next generation.



▶ Provivi

One of the biggest limitations to this new technology is high cost. However, Provivi synthesizes pheromones at large scale and reduced cost by using biocatalysts and low-cost raw materials.



Paradigm Shift



Traditionally insecticides have been designed to kill a pest. In this case it is different, since pheromones are applied to disrupt the mating process and keep the population low by diminishing the mating success.





Pheromones

- Since pheromones are biosynthesized by the different organisms they are specified for/by, they are usually environmentally benign, non-persistent, and highly specific (meaning they act at relatively low concentrations, and **only** on the target organism).

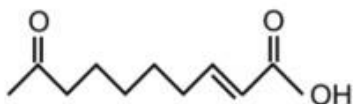
Silkmoth (*Bombyx mori*)
(E,Z)-10-12-hexadecadien-1-ol



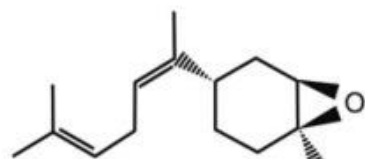
Gypsy moth (*Lymantria dispar*)
Disparlure (+)
(7R,8S)-cis-7,8-Epoxy-2-methyloctadecane



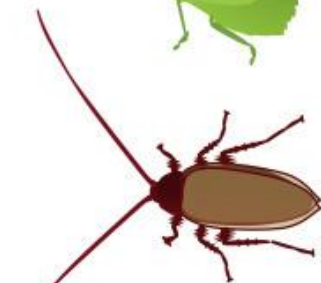
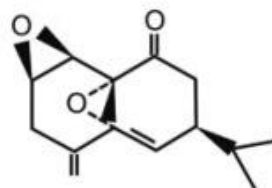
Honeybee (*Apis mellifera*)
(E)-9-oxo-2-decenoic acid



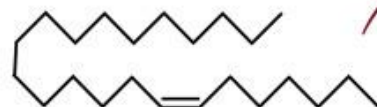
Green stink bug (*Nezara viridula*)
(1S,4S,6R)-1-methyl-4-
(Z)-6-methylhepta-2,5-dien-2-yl)-
7-oxabicyclo[4.1.0]heptane



Cockroach (*Periplaneta americana*)
Periplanone B
(1Z,5E)-1,10(14)-diepoxy-4(15),
5-germacradien-9-one



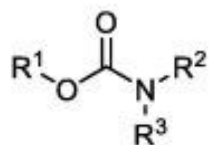
Fruit fly (*Drosophila melanogaster*)
7 tricosene, non volatile



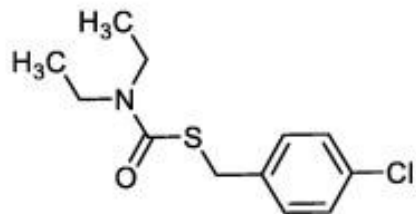
Structurally very different



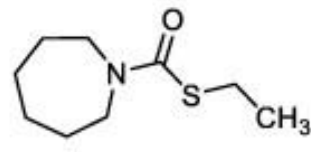
Pesticides are still almost exclusively of synthetic origin and some of them highly toxic, broadband, and structurally different than pheromones.



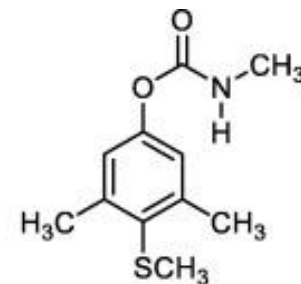
General carbamate structure



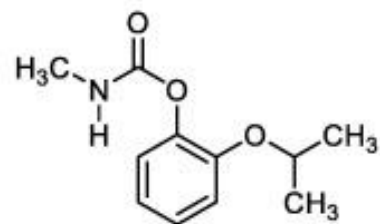
Thiocarbamates



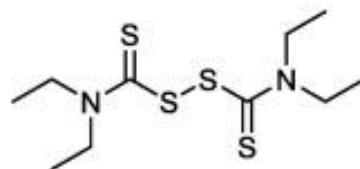
Molinate



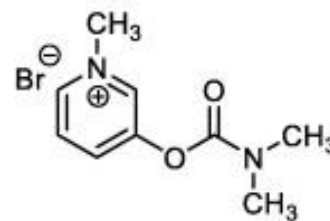
Methiocarb



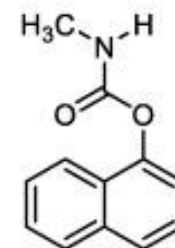
Propoxur



Disulfiram



Pyridostigmine



Carbaryl



Provivi uses Biocatalysis



- Biocatalysis is the approach that Provivi takes to synthesize their pheromones. They use enzymes that occur in nature (in microorganisms), study promising initial activities for their syntheses and then gradually increase the enzymes activities and selectivities to the desired level. This process is called **directed evolution** and can have a profound impact on the way we 'make' things.



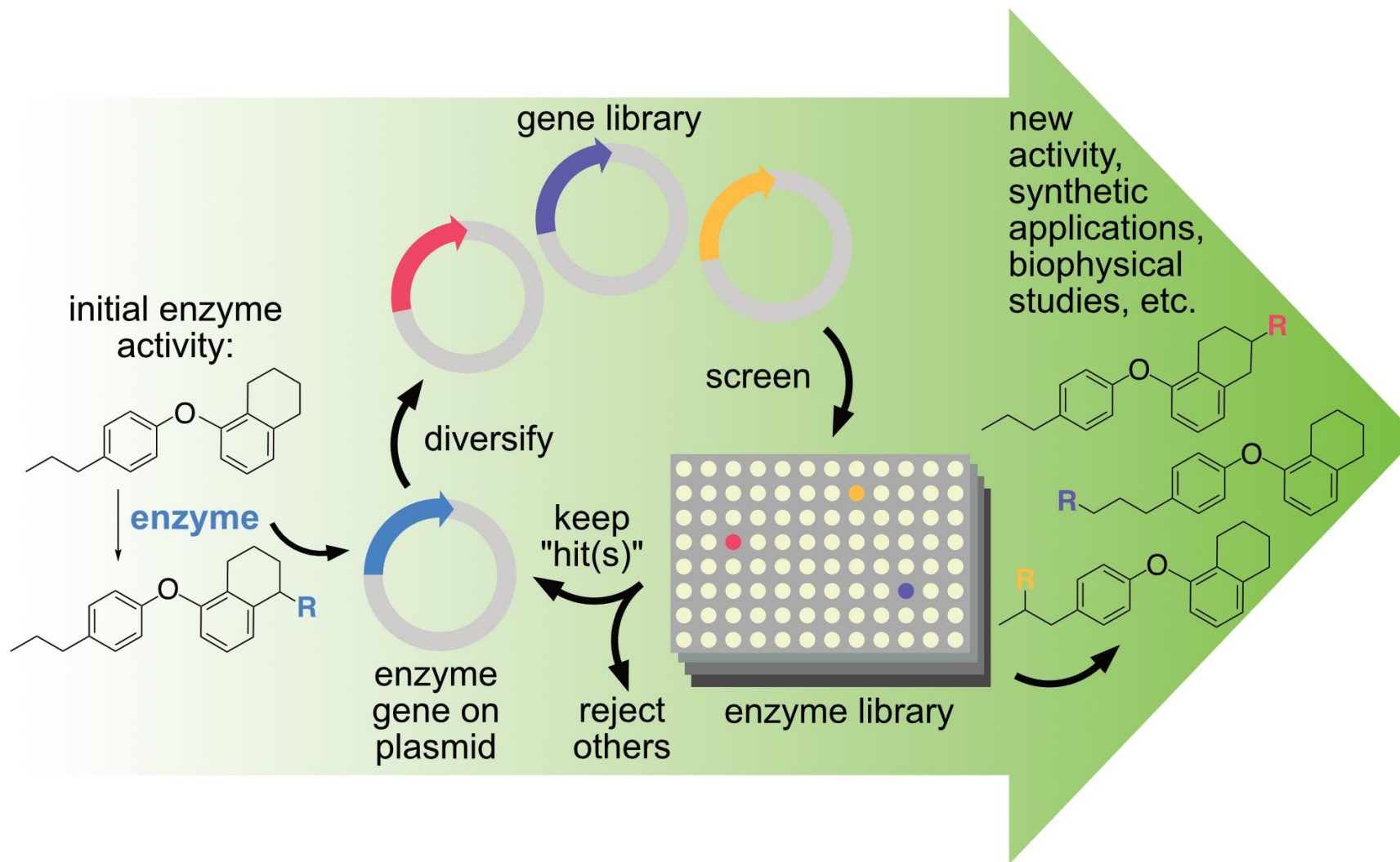
Credit: Caltech

Frances Arnold

- Co-Founder of Provivi
- Nobel Prize in Chemistry 2018 "Directed Evolution of Enzymes"



...and directed Evolution





Discussion

- Do we really need pesticides?
- How can we design even more benign pesticides?
- What can we do as consumers?
- How can governments support these efforts?





P2Science

P2



The complexity of cosmetics



Cosmetic chemical concerns



Some families of chemicals in personal care products cause concerns. Here we examine some of these ingredients' roles and why in some cases manufacturers are looking for alternatives.

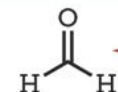


Cosmetic ingredient roles

Dyes or pigments	Color cosmetics
Emollients	Prevent water loss from the skin
Emulsifiers	Stop ingredients from separating
Fragrances	Improve the smell of cosmetic products
pH stabilizers	Adjust the acidity of cosmetics
Preservatives	Prevent the growth of microorganisms
Solvents	Dissolve other ingredients.
Thickeners	Increase the viscosity of cosmetics

Formaldehyde releasers

Preservatives

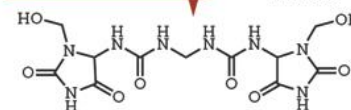


Formaldehyde

Formaldehyde releasers slowly generate the preservative formaldehyde. Though the levels of formaldehyde these compounds release are low, they can still cause an allergic response in sensitized people.

Imidazolidinyl urea

Formaldehyde releaser

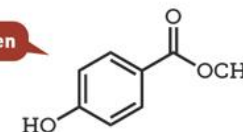


Parabens

Preservatives

Parabens are among the most effective preservatives but may mimic the hormone estrogen. The European Union restricts some parabens in cosmetics because of a lack of data from which to evaluate human risk. Regulators consider commonly used parabens, such as methylparaben, safe at typical cosmetic levels.

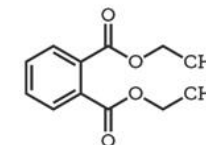
Methylparaben



Phthalates

Solvents and fragrance prolongers

Some phthalate esters may interfere with hormones and may have reproductive toxicity. Diethyl phthalate (DEP), used in some cosmetics, has less toxicity than longer-chain phthalate esters and is safe at the concentrations used.

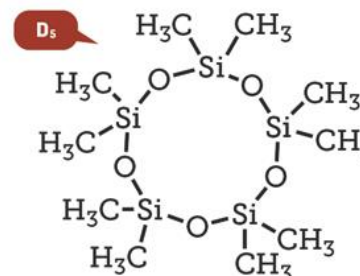


DEP

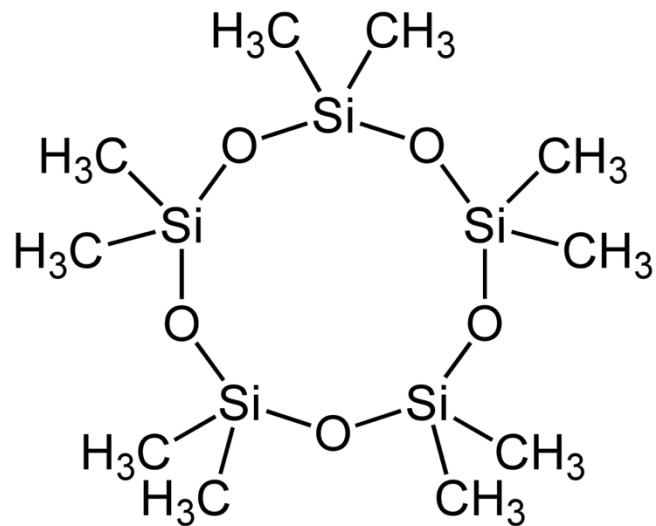
Silicones

Emollients and thickeners

Silicones in cosmetics include dimethicone and decamethylcyclopentasiloxane (D₅). The EU has limited the use of some cyclic silicones, including D₅, in cosmetic products because of concerns about their accumulation in the environment.

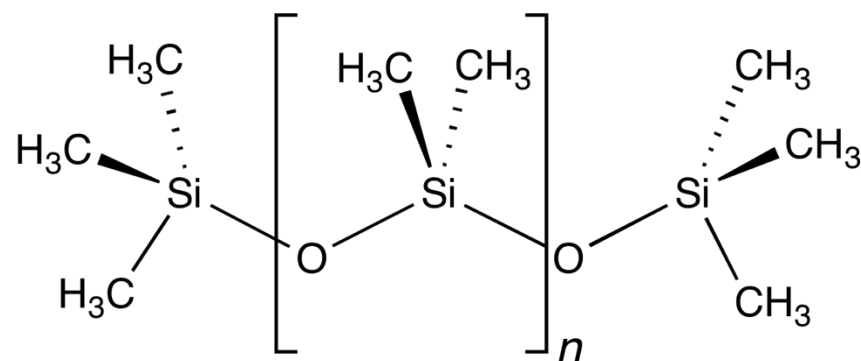


Silicones and emollients are problematic



Decamethylcyclopentasiloxane

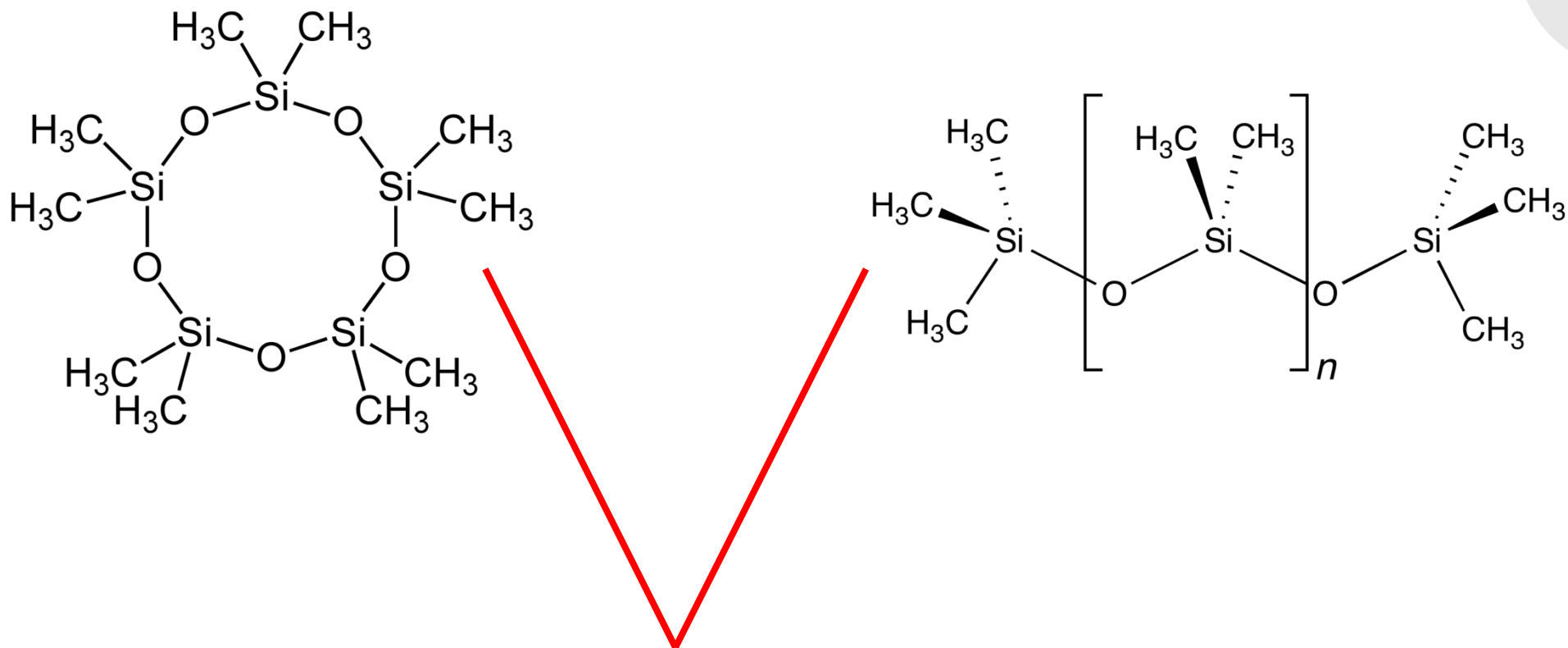
- volatile reagent used in deodorants for skin feel



Polydimethylsiloxane/Dimethicones

- liquid additives often used in formulations of hair products

Silicones and emollients are problematic



**Neither one was designed for degradability!
Both can cause problems for aquatic life.**



Silicones and emollients are problematic



Most skincare and cosmetic products are ending up in the waterways and treatment plants sooner or later. This increases the price for water treatment dramatically, and also causes problems for the environment and our overall water quality.



P2's Approach



P2 Science uses chemistry to transform terpenes from the forest and oleochemicals from the field into safe, renewable, high performance, biodegradable, and multi-functional new ingredients for flavors, fragrances, cosmetics, personal care products, and specialty materials.

Citropol® is a flagship of P2 Science's products. It is a novel class of low MW liquid polymers that are made from 100% forest-derived terpenes through a clean, mild, and high yielding conversion process.



Citropol Based-Products

Terpene derived cosmetic products are superior to traditionally used silicones and significantly less harmful to the environment, especially water streams.



P2's Approach



Citropol 1A vs Silicones

	Citropol 1A	Silicones
Biodegradable	✓	✗
Low-E-factor	✓	✗
Renewable	✓	✗
Clean label	✓	✗
Long-lasting	✓	✓
Non-greasy	✓	✓
Slippery	✓	✓

Cosmetics & Personal Care

Citrolatum® is a biorenewable, biodegradable, and biocompatible cosmetic semi-solid that is an alternative to petrolatum.

CitroButter™ is an all-natural butter that forms a protective layer on the skin and hair to prevent dryness and retain moisture.

And many more!

Important: these products are based on terpenes!

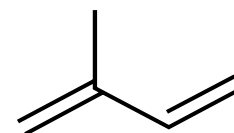


So what are terpenes?



More than 30,000 terpenes exist, most of them are produced by plants, especially by conifers and citrics.

They are all based on **Isoprene!**

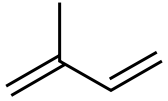


Isoprene

> 600 million tons of isoprene are emitted by plants each year

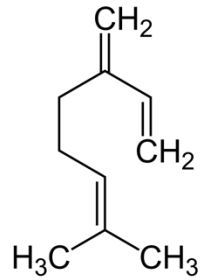


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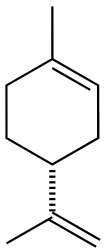


Isoprene

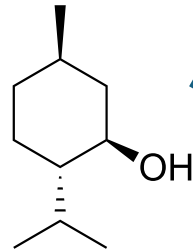
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Myrcene

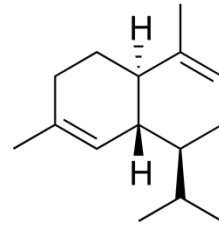


Menthol

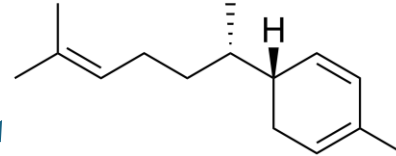


Limonene

Monoterpenes (n=2)

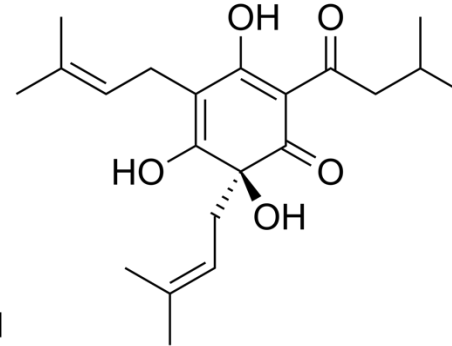


Cadinene

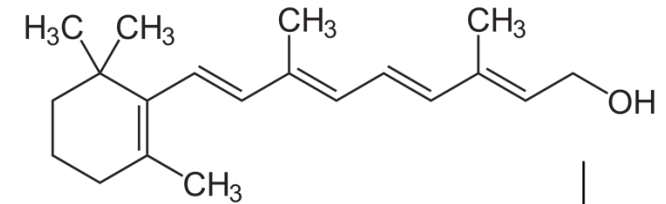


Zingiberene

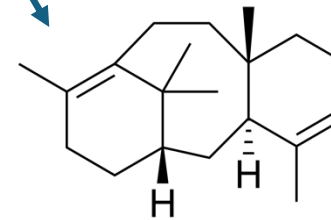
Sesquiterpenes (n=3)



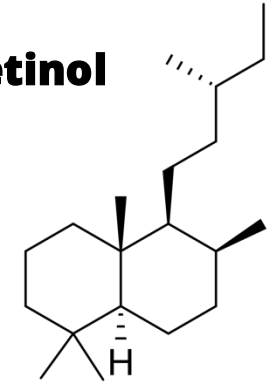
Humulone



Retinol



Taxadiene



Labdane

Diterpenes (n=4)

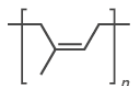


And they are everywhere



Male condoms are commonly made from latex. To avoid latex allergies, polyurethane condoms can be used instead; polyisoprene condoms are also available. Female condoms are made from polyurethane or nitrile rubber.

1855



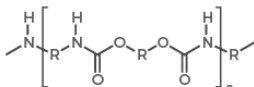
RUBBER

1920

A milky fluid mixture obtained from plants which contains rubber.

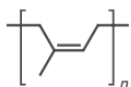
RUBBER LATEX

1994



POLYURETHANE

2008



POLYISOPRENE

(synthetic rubber)

Condoms protect against both pregnancy and sexually transmitted diseases. Studies show that polyurethane condoms are slightly more prone to breakage than latex ones.



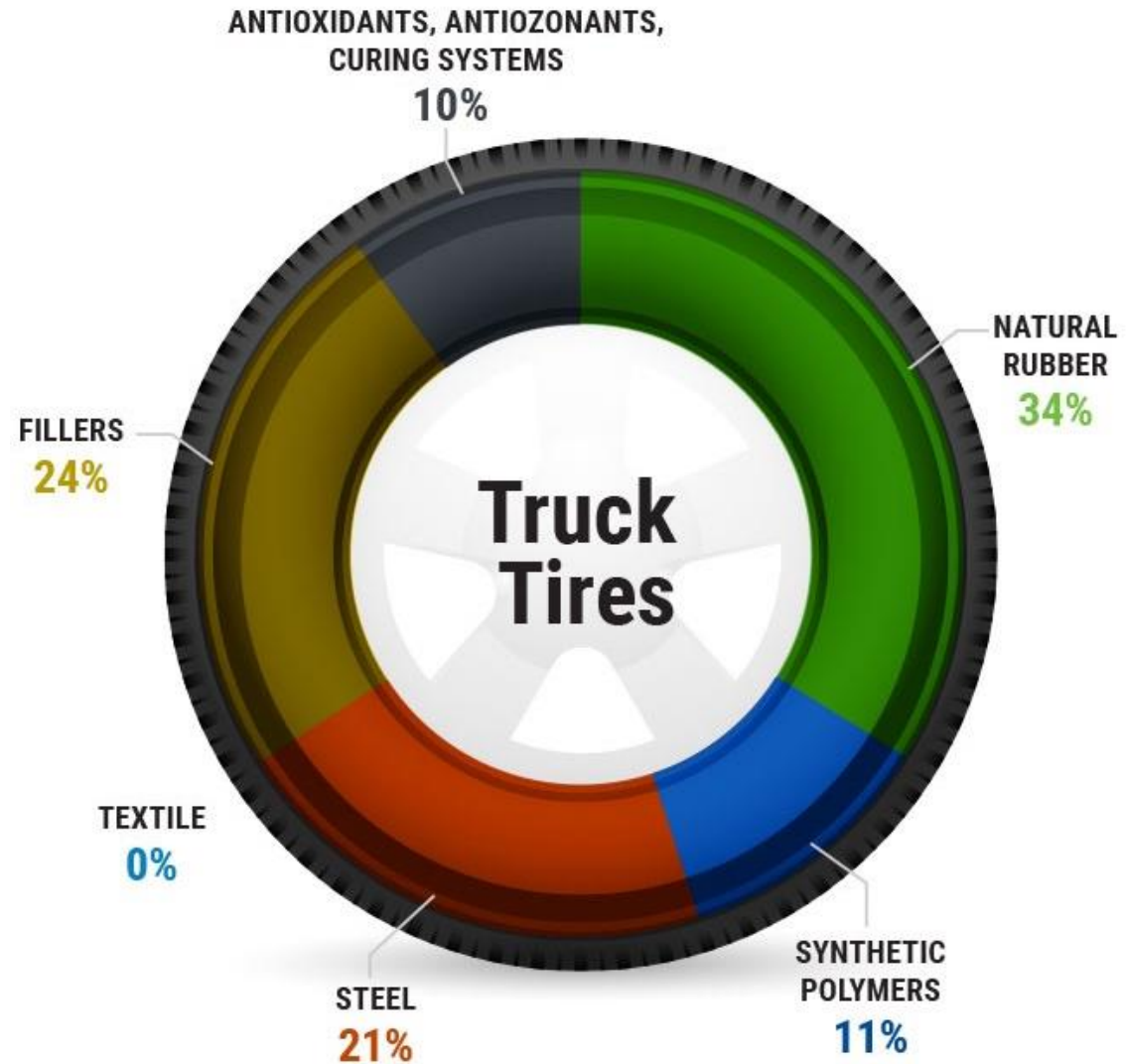
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And they are everywhere



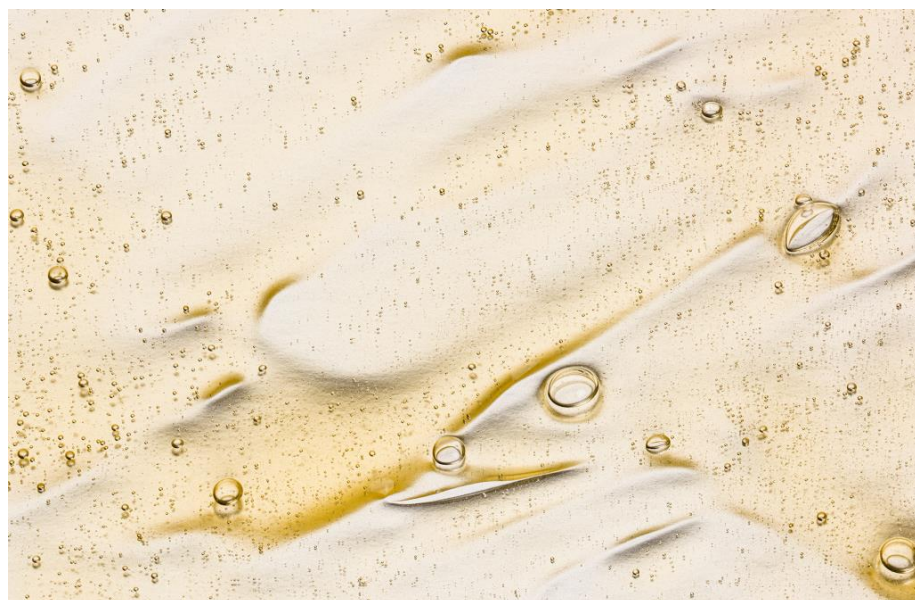
<https://www.ustires.org/whats-tire-0>



P2 Science's: Process Intensification



Although P2Science's processes are proprietary, they are based on the process intensification of terpene derivatizations.



Process Intensified Continuous Etherification (PICE™)



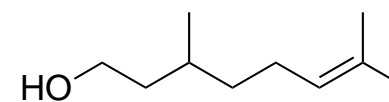
Process Intensified Ozonolysis (PIOz™)



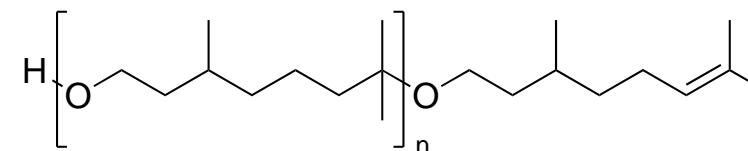
P2's Terpene-based polymers



Different grades of polymerization, *i.e.* different chain lengths, allow for the fine tuning of the mechanical and cosmetic properties.



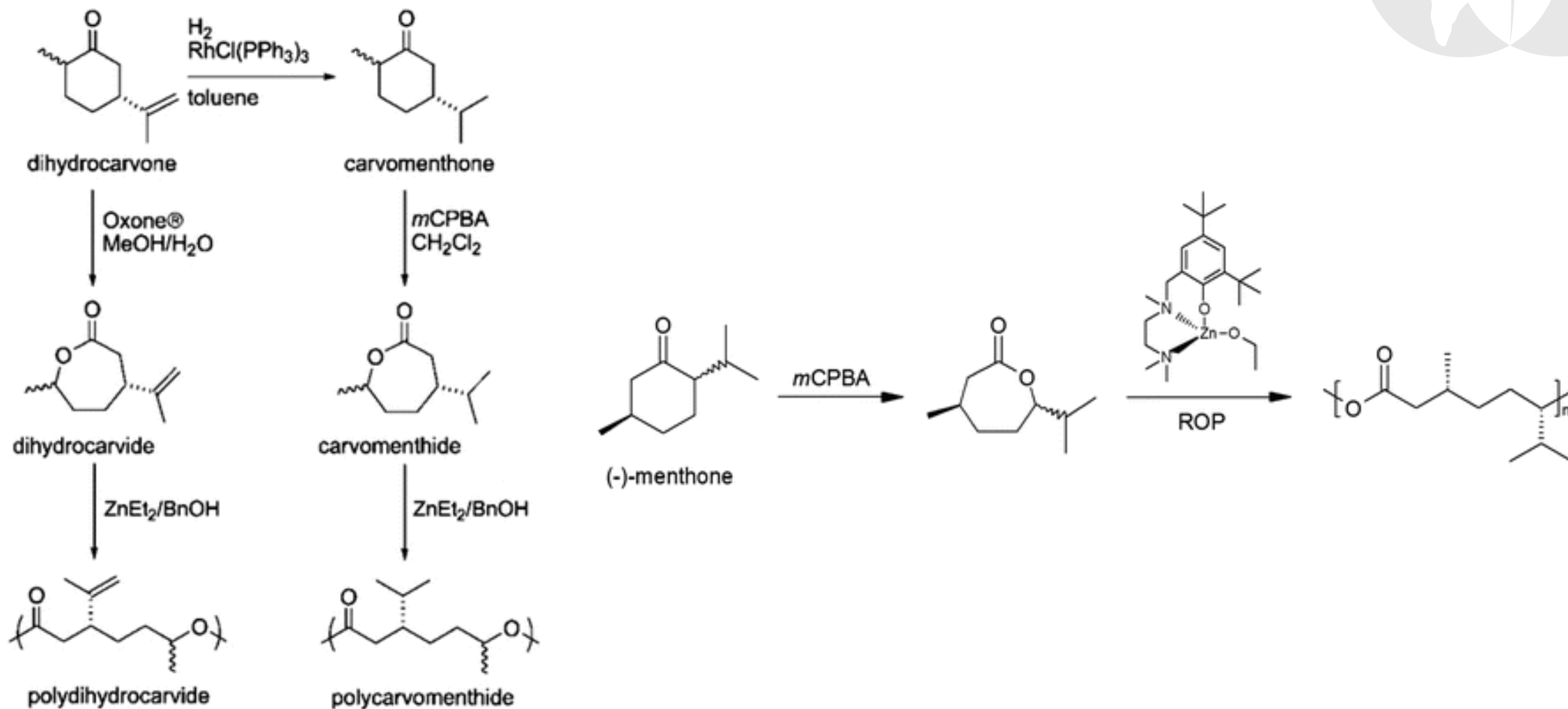
Citronellol



Polycitronellol



Other terpene-based polymers





Discussion

- What other steps could make cosmetics more benign?
- Can you imagine other biological feedstocks?
- What the consumer do?
- What is important to consider to protect our waters?





Yale School of
the Environment



Center for Green Chemistry &
Green Engineering at Yale

Advance Science

Catalyze
Implementation

Prepare the next
generation

Raise Awareness

Thank You!

For questions, please reach out:

✉ greenchemistry@yale.edu

<https://www.globalgreenchem.com>

📄 <https://www.chemistryforsustainability.org>

<https://greenchemistry.yale.edu/>



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